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CLAIMS

What is claimed is:

1. A chimeric antibody, comprising at least part of a human immunoglobulin constant region and at least part of a non-human immunoglobulin variable
5 region, said antibody capable of binding an epitope specific for human tumor necrosis factor TNF α .
2. A chimeric antibody according to claim 1, wherein said binding of said antibody to TNF α inhibits a pathologic activity of TNF α .
3. A chimeric antibody according to claim 1, wherein said antibody does not bind
10 to one or more epitopes included in amino acids 11-13, 37-42, 49-57 or 155-157 of SEQ ID NO: 1.
4. A chimeric antibody according to claim 1, wherein said chimeric antibody comprises two light chains and two heavy chains, each of said chains comprising
15 at least part of a constant region and at least part of a variable region, said variable region capable of binding an epitope of human TNF α .
5. A chimeric antibody according to claim 1, wherein said antibody neutralizes human TNF α under physiological conditions.
6. A chimeric antibody according to claim 1, wherein said variable region is of murine origin.

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7. A chimeric antibody according to claim 1, wherein said variable region is derived from a high affinity murine monoclonal antibody which binds to a neutralizing epitope of human $\text{TNF}\alpha$.
- 5 8. A chimeric antibody according to claim 7, wherein said murine monoclonal antibody competitively inhibits the binding of monoclonal antibody cA2 to $\text{TNF}\alpha$.
9. A chimeric antibody according to claim 1, characterized by an affinity, measured as an association constant (K_a), of at least 1×10^8 liter/mole.
- 10 10. A chimeric antibody according to claim 9, wherein said affinity, measured as an association constant (K_a), is at least 1×10^9 liter/mole.
11. A chimeric antibody according to claim 1, wherein said antibody neutralizes human $\text{TNF}\alpha$ with an ID_{50} of at least $1 \mu\text{g/ml}$.
12. A chimeric antibody according to claim 11, wherein said antibody neutralizes human $\text{TNF}\alpha$ with an ID_{50} of at least 15 ng/ml .
- 15 13. A chimeric antibody according to claim 12, wherein said antibody neutralizes human $\text{TNF}\alpha$ with an ID_{50} of at least about 100 ng/ml .
14. A chimeric antibody according to claim 1, wherein said antibody is in detectably labeled form.
- 20 15. A chimeric antibody according to claim 1, wherein said antibody is produced recombinantly.

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16. An immunoassay method for detecting human TNF in a sample, comprising:
 - (a) contacting said sample with an antibody according to claim 36, or a TNF binding fragment thereof, in detectably labeled form; and
 - (b) detecting the binding of the antibody to said TNF.
- 5 17. The chimeric antibody cA2.
18. A chimeric antibody, comprising at least part of a human IgG1 constant region and at least part of a non-human immunoglobulin variable region, said antibody capable of binding an epitope specific for human TNF α .
- 10 19. A chimeric antibody according to claim 18, wherein said binding of said antibody to TNF α inhibits a pathologic activity of TNF α .
20. A chimeric antibody according to claim 18, wherein said antibody does not bind to one or more epitopes included in amino acids 11-13, 37-42, 49-57 or 155-157 of SEQ ID NO: 1.
- 15 21. A chimeric antibody according to claim 18, wherein said chimeric antibody comprises two light chains and two heavy chains, each of said chains comprising at least part of a constant region and at least part of a variable region, said variable region capable of binding an epitope of human TNF α .
22. A chimeric antibody according to claim 18, wherein said antibody neutralizes human TNF α under physiological conditions.
- 20 23. A chimeric antibody according to claim 18, wherein said variable region is of murine origin.

24. A chimeric antibody according to claim 18, wherein said variable region is derived from a high affinity murine monoclonal antibody which binds to a neutralizing epitope of human $\text{TNF}\alpha$.
- 5 25. A chimeric antibody according to claim 24, wherein said murine monoclonal antibody competitively inhibits the binding of monoclonal antibody cA2 to $\text{TNF}\alpha$.
26. A chimeric antibody according to claim 18, characterized by an affinity, measured as an association constant (K_a), of at least 1×10^8 liter/mole.
- 10 27. A chimeric antibody according to claim 26, wherein said affinity, measured as an association constant (K_a), is at least 1×10^9 liter/mole.
28. A chimeric antibody according to claim 18, wherein said antibody neutralizes human $\text{TNF}\alpha$ with an ID_{50} of at least $1 \mu\text{g/ml}$.
29. A chimeric antibody according to claim 28, wherein said antibody neutralizes human $\text{TNF}\alpha$ with an ID_{50} of at least 15 ng/ml .
- 15 30. A chimeric antibody according to claim 28, wherein said antibody neutralizes human $\text{TNF}\alpha$ with an ID_{50} of at least about 100 ng/ml .
31. A chimeric antibody according to claim 18, wherein said antibody is in detectably labeled form.
- 20 32. A chimeric antibody according to claim 18, wherein said antibody is produced recombinantly.

33. An immunoassay method for detecting human TNF in a sample, comprising:
- (a) contacting said sample with an antibody according to claim 38, or a TNF binding fragment thereof, in detectably labeled form; and
 - (b) detecting the binding of the antibody to said TNF.

5 34. A chimeric antibody, comprising two light chains and two heavy chains, each of said chains comprising at least part of a human immunoglobulin constant region and at least part of a non-human immunoglobulin variable region, said variable region capable of binding an epitope of human tumor necrosis factor hTNF α ,
10 wherein said light chains comprise variable regions comprising SEQ ID NO: 3 and said heavy chains comprise variable regions comprising SEQ ID NO: 5.

35. A chimeric antibody according to claim 34, wherein the human immunoglobulin constant region is an IgG1.

15 36. A chimeric antibody comprising at least part of a human immunoglobulin constant region and at least part of a non-human immunoglobulin variable region, said antibody capable of binding an epitope specific for human tumor necrosis factor TNF α , wherein the non-human immunoglobulin variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 3 and SEQ ID NO: 5.

20 37. A chimeric antibody comprising at least part of a human IgG1 constant region and at least part of a non-human immunoglobulin variable region, said antibody capable of binding an epitope specific for human TNF α , wherein the non-human immunoglobulin variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 3 and SEQ ID NO: 5.

38. A chimeric antibody comprising at least part of a human immunoglobulin constant region and at least part of a non-human immunoglobulin variable region, said antibody capable of binding an epitope specific for human tumor necrosis factor $\text{TNF}\alpha$, wherein the non-human immunoglobulin variable region comprises a polypeptide encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO: 2 and SEQ ID NO: 4.
39. A chimeric antibody comprising at least part of a human IgG1 constant region and at least part of a non-human immunoglobulin variable region, said antibody capable of binding an epitope specific for human $\text{TNF}\alpha$, wherein the non-human immunoglobulin variable region comprises a polypeptide encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO: 2 and SEQ ID NO: 4.
40. A polypeptide comprising the amino acid sequence selected from the group consisting of SEQ ID NO: 3 and SEQ ID NO: 5 or at least one binding fragment thereof, wherein said polypeptide binds to $\text{hTNF}\alpha$.
41. A polypeptide of Claim 40, wherein said polypeptide neutralizes $\text{hTNF}\alpha$.
42. A polypeptide of Claim 40, wherein said polypeptide inhibits $\text{hTNF}\alpha$.
43. A polypeptide of Claim 40 which binds to at least one epitope included in amino acids 87-108, or both 59-80 and 87-108, of SEQ ID NO: 1.
44. A polypeptide of Claim 40 which does not bind to an epitope included in amino acids 11-13, 37-42, 49-57 or 155-157 of SEQ ID NO: 1.

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45. A polypeptide of Claim 40 which competitively inhibits the binding of monoclonal antibody cA2 to hTNF α .
46. A polypeptide comprising the amino acid sequence of SEQ ID NO: 3, wherein said polypeptide binds to hTNF α and competitively inhibits the binding of monoclonal antibody cA2 to hTNF α .
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47. A polypeptide comprising the amino acid sequence of SEQ ID NO: 5, wherein said polypeptide binds to hTNF α and competitively inhibits the binding of monoclonal antibody cA2 to hTNF α .
48. A polypeptide comprising at least one binding fragment of SEQ ID NO: 3, wherein said polypeptide binds to hTNF α and competitively inhibits the binding of monoclonal antibody cA2 to hTNF α .
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49. A polypeptide comprising at least one binding fragment of SEQ ID NO: 5, wherein said polypeptide binds to hTNF α and competitively inhibits the binding of monoclonal antibody cA2 to hTNF α .
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50. A polypeptide of Claim 45 having a hTNF α binding affinity, measured as an affinity constant (K_a), of at least 1×10^8 liters/mole.
51. A polypeptide of Claim 45 having a hTNF α binding affinity, measured as an affinity constant (K_a), of at least 1×10^9 liters/mole.
52. A polypeptide of Claim 45 which neutralizes hTNF α with an ID₅₀ of at least about 1 μ g/ml.
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53. A polypeptide of Claim 45 which neutralizes hTNF α with an ID50 of at least about 100 ng/ml.
54. A polypeptide of Claim 45 which neutralizes hTNF α with an ID50 of at least about 15 ng/ml.
- 5 55. A fusion protein comprising SEQ ID NO: 3 or SEQ ID NO: 5 or a binding fragment thereof, wherein said fusion protein binds to hTNF α .